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A CASE OF SPIRILLOSIS

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Much interest has recently been aroused in diseases from which curved organisms are isolated and we feel that the following case presents certain features which merit its report even though existing circumstances prevented the completion of the bacteriologic studies.

CLINICAL HISTORY

R. G., aged 22, of Italian extraction, crane operator, was admitted to the Allegheny General Hospital, Pittsburgh, April 16, 1917, service of Dr. James P. McKelvy, complaining of "stomach trouble." At this time the patient was able to walk. His family history was negligible. It appeared from his previous history, that he had been suffering from an intermittent unproductive cough accompanied by night sweats and gradual loss of weight and strength for several months, and that he had had several severe colds during the winter (1916-1917). Sore throat was not a prominent symptom of the colds. He had had gonorrhea in Dec., 1915, with good recovery. He gave no history of the usual exanthemata during childhood, but had had diarrhea at the age of 6 months which, according to his statement, had persisted for about 6 months. He denied syphilis and did not use alcohol.

The present illness began 7 months before admission with "cramps" in the region of the stomach which were aggravated by eating and lasted but a short time. As the disease progressed, the cramps became more severe after meals, varying in duration from a few minutes to several hours. The pains were relieved, as a rule, by a movement of the bowels. The stools were loose and watery. The diarrhea would entirely disappear on abstinence from food and drink. Meat particularly aggravated the symptoms. There was no bleeding, vomiting, headache or jaundice. There were no acute cardio-respiratory symptoms and the patient said there was no fever until a week before admission.

The patient did not look acutely ill. The skin and mucous membranes were pale and there was a general sallow appearance. The nutrition was below par. The eye reflexes were normal and there was no icterus of the sclerae. The mouth, ears and nose were normal. Several enlarged superficial glands were felt in the posterior cervical region, especially on the left side. The axillary lymph nodes and right epitrochlear nodes were definitely palpable. The parotid, submaxillary and thyroid glands were normal.

No definite consolidation could be found in the lungs although large and small moist râles were present in both lower axillae and in both bases.

The point of maximum intensity of the heart beat was in the 5th left intercostal space $9\frac{1}{2}$ cm. from the midline. No thrills or shocks were palpable. There was a systolic murmur at the apex, slightly transmitted to the axilla. There was also a systolic murmur at the base maximal along the sternal

border at the pulmonic area, and well transmitted toward the neck. The heart action was regular. The pulse was regular in force and rhythm, of good volume and of fair tension. The blood pressure was 105 mm., the diastolic 40 mm., and the pulse pressure 65 mm., or 162%. The vessel walls were not appreciably thickened.

The abdomen was distended and tympanitic, the muscles were held somewhat rigidly so that the position of the organs was unsatisfactorily made out. The spleen was just palpable, the liver edge not felt. There were no masses or localized areas of tenderness. Examination of the extremities showed tenderness on pressure over the middle of the right tibia. The knee kicks were decreased. There was no edema, redness, swelling, sensory disturbances or abnormal reflexes.

The tentative diagnosis was typhoid fever. Blood cultures and agglutination tests on April 7, 14, and 21, yielded negative results. The urine was negative. Culture from the urine on April 22 was negative. Blood examination on March 22 (Dr. Willetts) showed red blood cells 3,700,000; white blood cells, 9,200; hemoglobin, 63% (Sahli); differential leukocyte count—polymorphonuclear leukocytes, 63%; lymphocytes, 19%; large mononuclears, 12%. The red blood cells showed marked anisocytosis, some poikilocytosis, some anisochromia, very slight polychromatophilia, no stippling, no nucleated forms and few blood platelets. The Wassermann reaction was negative.

After some days, an area of high pitched tympany developed in the left axilla, extending somewhat anteriorly and there were signs of a diffuse bronchitis. There was an area about the apex of the heart and over the whole right base of increased breath sounds, whispered and spoken voice sounds, prolonged expiration and bronchovesicular breathing. On April 21, there was a striking enlargement of the submaxillary, posterior cervical, axillary, epitrochlear, and inguinal glands which lasted but a few days. There was no tenderness of the involved glands. The spleen became definitely palpable. There were a number of small, pea-sized nodes palpable in the anterior axillary line and along the margin of the pectoralis muscle. The temperature gradually came down to normal on April 25, and remained so until May 3. Intradermal tuberculin tests with 1/100 mg., 1/10 mg. and 1 were negative. On April 27, an acute otitis media developed on the left side necessitating incision. On April 29, an injection of $\frac{1}{33}$ grain of atropin sulphate showed a change in pulse from about 100 to 120 per minute. On April 30, a blood count showed red blood cells, 2,000,000; white blood cells, 3,200; and hemoglobin, 30% (Sahli). On May 3, a marked swelling and tenderness on the left cheek developed which gradually disappeared under cold applications. On May 6, considerable tenderness appeared along the left femoral artery and in the adjacent muscles; no edema of the foot developed and arterial pulsation persisted. This condition cleared up after several days. A period of diarrhea then occurred, with distention of the abdomen. The fever continued, the loss of weight was marked the patient became dull and drowsy and at times obstinate and combative. The abdomen then became scaphoid and generally tender, but the reflexes remained present and active. There were abnormal reflexes in the extremities. The neck was held rather rigidly but was not painful. On May 14, a blood count showed red blood cells, 848,000; white blood cells, 1,500; hemoglobin, 10% (Sahli). The red blood cells showed considerable anisocytosis, poikilocytosis and slight anisochromia, but were generally of a good color. No abnormality was noted in the white blood cells except perhaps an increase in the number of mononuclear cells. No pigmented cells were seen. On May 10, a blood culture was taken, which after 5 or 6 days'

incubation showed the presence of a very actively motile curved organism. On May 14, the patient died.

Cultures taken during the necropsy yielded organisms identical with those isolated before death.

BACTERIOLOGIC EXAMINATION

The organisms isolated before death appeared in dextrose broth, serum broth and in deep agar cultures. Culture of the heart blood at necropsy

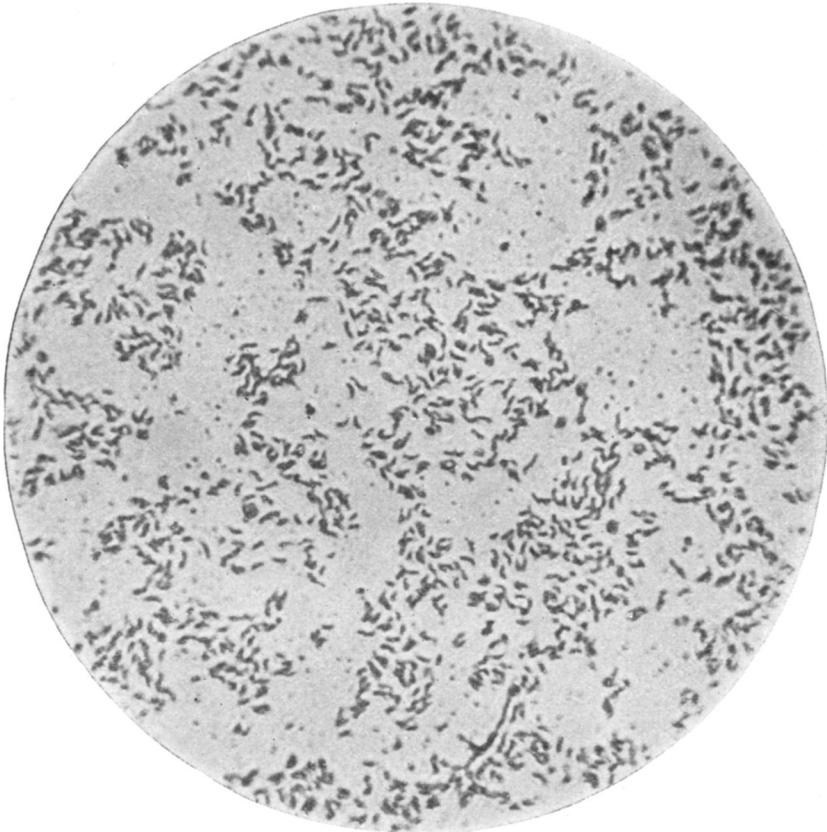


Fig. 1.—Comma-shaped organisms from freshly isolated cultures.

yielded similar organisms in dextrose broth, lactose broth, Noguchi tissue broth and on blood agar. Cultures from the spleen, lymph nodes, urine and pleural fluid were negative.

Transfers were made from these fluid cultures to plain agar, blood agar and Loeffler's blood serum. No growth occurred on plain agar, but on the 3rd or 4th day, very fine moist colonies were found on the Loeffler serum and blood agar. The organism grew rapidly well under anaerobic and aerobic conditions. After being kept on solid mediums for a few weeks the cultures became

luxuriant and colonies were visible in 48 hours after transfer. It was necessary to plant them every 10 days or 2 weeks to keep the cultures living. Transfers made to carbohydrate broths and milk at this time showed a very slight amount of growth. After 6 months (May-October) transfers made to the same mediums produced in 48 hours a marked turbidity but no acid or gas. After 2 weeks on the litmus milk there occurred peptonization and precipitation without any change in the reaction and without coagulation. No indol was formed.



Fig. 2.—Well developed spirilla found after several transplants on artificial mediums.

Microscopically, the organisms were interesting because of the changes in morphology which occurred from time to time. In the freshly isolated cultures they appeared as short, commalike bodies, having from 1-3 curves (Fig. 1). After a few transfers, a predominance of long, slightly spiral, threadlike bodies were found (Fig. 4), while subsequent transfers showed types, varying from the short vibrios to the long threadlike forms, with many intermediate stages (Fig. 3). In some cultures definite spirilla were found (Fig. 2).

Inoculations of rabbits, guinea-pigs, white rats and white mice failed to throw any light on the character of the organism. It is probable that repeated inoculations, or the use of a greater variety of animals, would have been of value. Forty-eight hour growths on blood-agar slants were washed off with salt solution and the growth from a single slant used as the dose. Full doses were given to each of 3 rabbits intravenously, and in 4 guinea-pigs and 1 white rat intraperitoneally. Half doses were injected intraperitoneally into



Fig. 3.—Cultures showing various types.

2 white mice. All of the animals were observed for a period of more than 6 weeks and none of them showed any untoward effects.

POSTMORTEM EXAMINATION (DR. HAYTHORN)

The body was greatly emaciated, severely anemic, with general glandular enlargement. About 300 cc of clear fluid present in the left pleural cavity. The right lung adherent. Both pleural surfaces covered with petechial hemorrhages. Both lungs pale, edematous, and contained healed tubercles. The peribronchial lymph nodes anthracotic and contained healed tubercles. The

pericardial sac contained over 100 cc of clear fluid. The epicardium smooth and glistening. The subepicardial fat showed serous atrophy. The right side of the heart dilated; myocardium pale and edematous. The endocardial surfaces and valves normal. The aorta was surrounded with a mass of grayish-brown lymph nodes, firm and fibrous. The aortic wall thickened, inelastic and showed irregular linear intimal sclerosis, most marked in the arch. The abdominal cavity contained 2000 cc of clear straw colored fluid. The fat was almost entirely absent. The lower border of the liver was 10 cm.

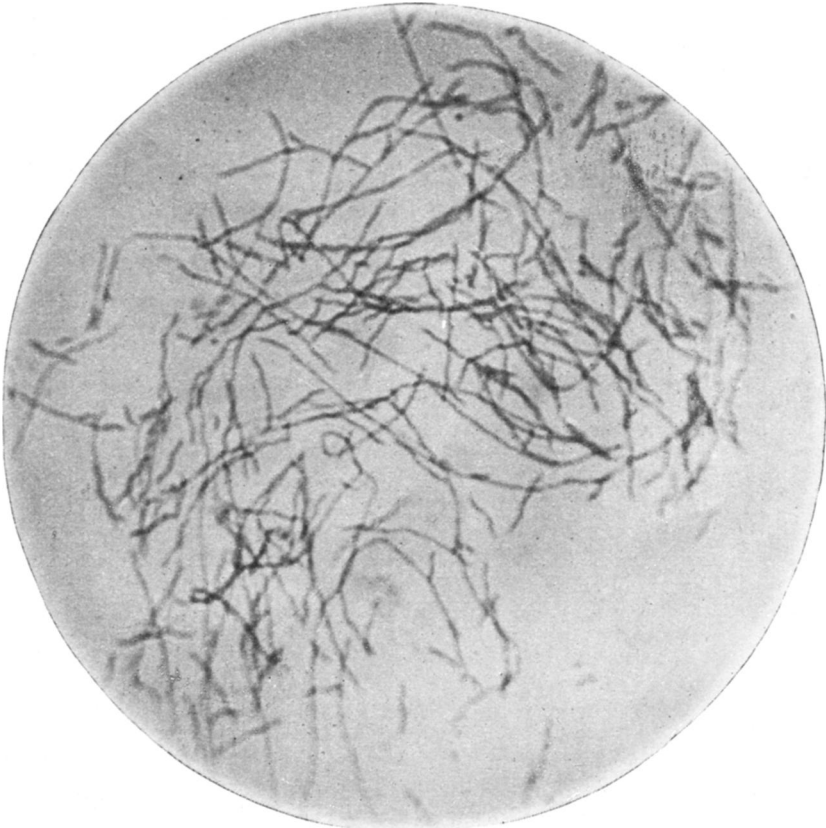


Fig. 4.—Threadlike forms developed after several days on artificial mediums.

below the costal margin. Adhesions between the colon and gallbladder. The mesenteric and retroperitoneal lymph nodes enormously enlarged. The spleen weighed 1,160 gm. and contained multiple infarcts. The pulp soft and purplish-red in color. The splenic artery and vein free from thrombi and sclerosis. The mucous membrane of the stomach was pale and many minute superficial more or less puckered ulcers were present. The small intestine showed nothing of interest. The colon was covered with a finely granular exudate and the walls were edematous. The liver weighed 1,920 gm. The

capsule showed many white linear thickenings; the cut surface mottled, pale tan and white, with some hemorrhagic spots. The gallbladder and ducts normal. The pancreas weighed 110 gm. and was edematous. The adrenals normal. The kidneys weighed 220 and 200 gm., respectively; capsules adherent; the cortical surfaces showed a few petechial hemorrhages; the cortex pale and swollen; the glomeruli seen with difficulty. The pelvic mucosa contained petechial hemorrhages. The other genito-urinary organs showed no particular changes. The marrow in the vertebrae was semisolid and of a magenta red color; that of the femur bright red, hemorrhagic and soft; there was no marginal area of spongy bone and no evidence of bony absorption.

Microscopically the heart muscle cells were markedly infiltrated with fat granules and a general degenerative myocarditis was present. The aorta presented a marked intimal and subintimal sclerosis with destruction of the elastic layers and connective tissue replacement. There was edema and anthracosis of the lungs with fresh hemorrhagic foci on the pleura. Sections from the ulcerated areas of the stomach were in general suggestive of those of the intestine in early typhoid fever: They were characterized by destruction of the glands in the lower layers of the mucosa accompanied by both hyperplasia and infiltration of endothelial cells. The latter were phagocytic for red cells, cellular debris and chromatin substances. The submucosa was also invaded but the muscular layers apparently free from inflammatory exudate. The pancreatic trabeculae were infiltrated with lymphocytes. The liver was edematous, the cells greatly compressed and elongated. The sinusoids were dilated and free from red cells. The periportal connective tissue appeared much compressed and thickly infiltrated with lymphocytes, plasma and endothelial cells. The lobules were distended and the peripheral portions seemed to be fairly well preserved. Some of the cells gave a faint reaction for hemosiderin. The central and midzonal areas contained foci of necrosis in which the liver cells had either entirely disappeared or were decreased in number. Such foci were extensively infiltrated with phagocytic endothelial cells, lymphocytes, plasma cells, and a moderate number of neutrophils. The endothelial cells contained entire cells, cellular debris and comma-shaped bits of material believed to be spirilla. Cocci were present in small numbers. The process, while generally focal, was also more or less diffuse. Many of the endothelial cells gave a very decided iron reaction, and all of the remaining liver cells gave a strong red reaction for granular fat with sudan III. A few focal necroses were present in the adrenals. The kidneys were edematous; the tubular epithelium atrophied and reacted positively for fat; hyalin and blood casts were present. The testes were edematous. The spleen was congested and infarcted. Several thrombosed vessels were present and the general picture was that commonly seen in acute septic conditions. Nestlike phagocytes filled with red blood cells and debris were abundant and questionable comma-shaped organisms numerous. The marrow was largely made up of a waxy homogeneous nonnucleated material; where less injured marrow persisted the tissue was infiltrated with phagocytes. Many bacteria, either short chains of cocci or spirilla, were found both within cells and free in the substance. No normal areas were found. The lymph nodes presented granulomatous changes, the germ centers being destroyed and replaced by a loose vascular stroma, which was more or less hyaline in places; the tissue was infiltrated with large single and multinucleated cells (having from 2-6 nuclei) which showed no necrosis and were intensely phagocytic for cells, debris and spirilla. The process was suggestive of, but not identical with, the

Dorothy Reed type of Hodgkins disease. The findings in the nodes may be summarized briefly as that of a diffuse sclerosing process with tumorlike giant cells caught in the new formed tissue meshes.

SUMMARY

The occurrence, in a young Italian, of a recurrent fever characterized by acute exacerbations, accompanied by severe secondary anemia, general lymph node involvement, splenomegaly and varying lung symptoms, and the isolation from the blood both during life and at necropsy of a motile curved organism are the salient features of the case.

The resemblance to typhoid fever during the earlier course of the disease was striking save that all of the laboratory tests were consistently negative. The next tentative diagnosis was that of a generalized tuberculosis, but this was not corroborated by tuberculin tests and further observations. The most unusual feature was the sudden enlargement of the lymph nodes with subsidence within a few days to a more nearly normal size. A study of the sections suggests that enlargement was due to a severe inflammation of the intranodal sinuses which healed by granulomatous changes leading to extensive connective tissue development. The progressive secondary anemia was extreme, and there were no evidences of blood regeneration found either in the blood examinations or in the sections of the marrow. The marrow was red but the sections showed the color to be due to necrosis and hemorrhage and not to hyperplasia. The hemosiderin in the liver and spleen as well as the extreme phagocytosis of red cells in the latter showed that the anemia was due not only to the failure in production of red cells, but also to actual blood destruction in the tissues. The splenomegaly was probably secondary to the anemia. A few small foci of nodular connective tissue, slight edema and the pleural hemorrhages were all that were present at necropsy to explain the lung symptoms. Anatomic changes associated with the diarrhea and general toxic condition were seen in the stomach ulcers, the membrane in the colon and in the necroses of the liver. The main point of interest is, of course, the isolation both before and after death of an actively motile, spirally curved organism from the blood. This spirillum grew equally well aerobically and anaerobically. Just where it should be classified among spirally curved organisms we are not prepared to say.